Received: 4 May 2020 | Revised: 1 June 2020 | Accepted: 8 June 2020

DOI: 10.1111/odi.13496

ORAL DISEASES Leading in Oral, Maxillofacial, Head & Neck Medicine WILEY

LETTER TO THE EDITOR

Altered taste in patients with COVID-19: The potential role of salivary glands

Dear Editor,

The novel coronavirus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) constitutes a public health emergency of international concern. Taste and smell disorders have been reported along with various other clinical problems. In some studies (Fitzgerald, 2020; Machado & Gutierrez, 2020; Parma et al., 2020; Yan, Faraji, Prajapati, Boone, & DeConde, 2020), smell and taste disturbances have been reported in COVID-19-positive subjects, suggesting that chemosensory dysfunction should be considered when screening for this disease. In this manuscript, the possible influence of salivary gland dysfunction and hyposalivation in the chemosensory disorders observed in COVID-19 patients is briefly discussed.

SARS-CoV-2 uses angiotensin-converting enzyme-2 (ACE2) as an important receptor for entry and transmembrane serine protease 2 (TMPRSS2) for priming (Hoffmann et al., 2020). In addition, the spike viral protein of SARS-CoV-2 appears to be depended on sialic acid-rich proteins and gangliosides GM1 for coupling (Fantini, Di Scala, Chahinian, & Yahi, 2020). Gangliosides GM1 have an important role in many cellular processes facilitating pathogen entry (Schnaar, 2019). Saliva, a biological fluid produced by the major and minor salivary glands, contains water, ions, and several protein groups, including mucins, which have sialic acid in its composition (Shogren, Gerken, & Jentoft, 1989). The salivary glands were shown to present ACE2 (Liu et al., 2011; Xu, Li, Gan, Du, & Yao, 2020), TMPRSS2 (Vaarala, Porvari, Kellokumpu, Kyllönen, & Vihko, 2001), and gangliosides GM1 (Nowroozi, Kawata, Liu, Rice, & Zernik, 2001). Taken together, these demonstrate the possibility of salivary gland infection by SARS-CoV-2 (Chen, Zhao, et al., 2020).

Hyposalivation was hypothesized to expose patients to a higher risk of contracting COVID-19, as the reduction in saliva secretion may impair the secretion of antimicrobial proteins and peptides that illustrate antiviral activity, particularly against coronaviruses (Farshidfar & Hamedani, 2020). Hyposalivation, a condition that has been mostly reported as an adverse effect of drugs, radiotherapy of head and neck tumors, and Sjögren's syndrome (Villa, Connell, & Abati, 2015), can also be caused by infectious and inflammatory processes. Thus, salivary gland infection driven by SARS-CoV-2 might also affect saliva secretion. Hyposalivation and disturbances in salivary biomarkers may cause xerostomia (Farsi, 2007; Romero, Ibuki, & Nogueira, 2012), which has been associated with oral sensorial complaints (Mortazavi, Baharvand, Movahhedian, Mohammadi, & Khodadoustan, 2014). Moreover, oral neuropathy or neurological transduction interruption induced by salivary compositional alterations is responsible for oral sensory complaints and loss of taste function (Henkin, 1999; Hershkovich & Nagler, 2004). Psychological factors may also affect salivary flow rate and composition (M Bergdahl & Bergdahl, 2000; Gholami, Sabzvari, Razzaghi, & Salah, 2017), and thus, the psychological effects of the COVID-19 (Dong & Bouey, 2020; Duan & Zhu, 2020) on salivary gland secretion and taste disturbances (Maud Bergdahl & Bergdahl, 2002) could not be ignored.

Coronaviruses, including SARS-CoV-2, have neuroinvasive capacities since they can spread from the respiratory tract to the central nervous system (Desforges, Le Coupanec, Stodola, Meessen-Pinard, & Talbot, 2014; Li, Bai, & Hashikawa, 2020). In addition, there are reports of cranial nerve involvement and neurologic manifestations of SARS-CoV-2 (Troyer, Kohn, & Hong, 2020; Vonck et al., 2020). The reported taste disturbances in COVID-19-positive subjects have only been subjective in nature, and it remains unknown if patients have actual disturbances in their sense of taste or whether they are experiencing a disturbance in flavor, which is a combination of olfactory, gustatory, and trigeminal inputs (Bromley, 2000; Fitzgerald, 2020; Parma et al., 2020; Yan et al., 2020). SARS-CoV-2 is capable of directly infecting olfactory neuroepithelium, which is the prevailing theory for taste dysfunction (Chen, Shen, et al., 2020; Fodoulian et al., 2020). Thus, taste alterations resulting from the direct effect of SARS-CoV-2 infection on sensory neurons or other components of the peripheral gustatory system should also be considered.

Therefore, salivary gland infection and consequent disturbances in salivary flow rate and composition might be among the possible causes of taste alterations caused by SARS-CoV-2. Since the pathophysiology of COVID-19 remains not fully elucidated, studies are necessary to understand the real role of salivary glands and saliva in the taste alterations observed in COVID-19 patients.

CONFLICT OF INTEREST

The author declare no potential conflict of interest with respect to the authorship and/or publication of this article.

AUTHOR CONTRIBUTION

Marlus da Silva Pedrosa: Conceptualization; Data curation; Formal analysis; Methodology; Supervision; Validation; Visualization; Writing-original draft; Writing-review & editing. **Carla Renata Sipert:** Conceptualization; Supervision; Writing-review & editing. **Fernando Neves Nogueira:** Conceptualization; Supervision; Writing-original draft; Writing-review & editing.

FUNDING INFORMATION

This study was supported by the São Paulo Research Foundation (No. 2019/14556-7) and scholarship from the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—CAPES.

Marlus da Silva Pedrosa[1]
Carla Renata Sipert[2]
Fernando Neves Nogueira[1]

[1]*Department of Biomaterials and Oral Biology, Faculdade de Odontologia – Universidade de São Paulo (USP), São Paulo, SP, Brazil*
[2]*Departament of Restorative Dentistry, Faculdade de Odontologia – Universidade de São Paulo (USP), São Paulo, SP, Brazil*

Correspondence
Marlus da Silva Pedrosa, Departmento de Biomaterais e Biologia Oral of Biomaterials and Oral Biology – Faculdade de Odontologia – Universidade de São Paulo (USP), Av. Prof. Lineu Prestes, 2227 – Cidade Universitária, São Paulo – SP – Braszil – 05508-900
Email: marlus@usp.br

ORCID

Marlus da Silva Pedrosa https://orcid.org/0000-0002-4052-7208
Carla Renata Sipert https://orcid.org/0000-0002-5719-6505
Fernando Neves Nogueira https://orcid.org/0000-0002-6595-9154

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